

AMENDMENT UNDER 37 C.F.R. § 1.11  
U.S. Application No.: 10/671,546

Attorney Docket No.: Q77645

AMENDMENTS TO THE DRAWINGS

Please replace Figs. 1-4 with the replacement drawings submitted herewith. No new matter has been added.

Attachments: Two (2) Replacement Sheets (Figs. 1-4)

**REMARKS**

By this Amendment, claims 5-8 are added for examination, therefore, claims 1-8 are all the claims pending in the application.

The Examiner incorrectly requires that the foreign priority document be referenced in the application.

The drawings are objected to under 37 C.F.R. 1.83(a) because they fail to show “x axis” and “y axis” labels as described in the Specification.

Claims 1-4 are rejected under 35 U.S.C. 101.

Claims 1-4 are rejected under 35 U.S.C. 112, second paragraph.

Claims 1 and 3 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps.

Claims 3 and 4 are rejected under 35 U.S.C. 102(a) and (e) as being anticipated by Li et al. (U.S. Patent No. 6,571,005).

Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Li et al. (U.S. Patent No. 6,571,005), in view of Tseng et al. (Nucleic Acids Research, 2001, Vol. 29, No. 12, pp. 2549-2557) and Quackenbush (Nature, 2002, p. 496).

Claims 1-2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tseng et al. (Nucleic Acids Research, 2001, Vol. 29, No. 12, pp. 2549-2557), in view of Alon et al. (Proc. Natl. Acad. Sci., 1999, Vol. 96, pp. 6745-6750).

The Applicants traverse the rejections and request reconsideration.

***Interview Summary***

The Applicants thank the Examiner for the discussions during the telephonic interview on March 8, 2006 for clarifications in the Office Action dated February 10, 2006. The Applicants thank the Examiner for providing a new Office Action to clarify the issues discussed during the telephone interview and for resetting the due date for responding thereto. No other substantive issues other than clarifying the column and line numbers of the primary reference Li were discussed.

***Priority Document***

The Examiner requires that the Applicants include a first sentence containing the priority information. However, the Examiner is believed to be mistaken in his characterization of the law. Such a requirement is only in case of domestic priority (for example, continuations, continuation-in-part, etc). Therefore, the Examiner is requested to withdraw the requirement.

***Drawings and clarifications related to Fig. 3 & 4***

The Examiner alleges that the axes in the figures are not marked. The Applicants respectfully submit that the axes are clearly marked as 1 and 2. Further, the relation between the axes and the sample values are also clearly discussed in the Specification.

For example, as noted in pages 14-15, in Fig. 1, axis 1 corresponds to  $\log x$ , where  $x$  is an expression quantity of the first sample. Likewise, axis 2 corresponds to  $\log y$ , where  $y$  is an expression quantity of the second sample.

Likewise, in Fig. 2, the axis 1 corresponds to  $\log x$  and axis 2 corresponds to  $\log y'$ , where  $y' = 10^a$ . To further clarify, the Applicants rename axis 2 in Fig. 2 as 2' since this is different from axis 2 of Fig. 1.

Like for Figs. 1 & 2, the Applicants rename axis 2 in Fig. 4 as 7' for the same reasons and the Examiner is referred to page 18 of the Specification for further discussions.

***Amendments to the Specification***

The Applicants also amend the Specification to further clarify the subject matter and rectify certain typographical errors. No new matter is added.

***Claim rejections under 35 U.S.C. § 101***

In rejecting the claims under section 101, the Examiner notes processed may be statutory where they recite a concrete, tangible and useful result. However, the Examiner incorrectly concludes that the claims do not result such a concrete, tangible and useful result.

The Examiner's assertion of the subject-matter of the present invention being directed to non-statutory subject matter is based on an improper application of the USPTO Guidelines revised subsequent to the decision in *Ex parte Lundgren*, Appeal No. 2003-2088. (See generally Guidelines101\_20052026.pdf which can be located at [www.uspto.gov](http://www.uspto.gov))

An invention falls within the scope of the subject matter under 35 U.S.C. § 101 if what is claimed "physically transforms an article or otherwise produces useful, concrete and tangible result." According to the new USPTO Guidelines, first, an Examiner should determine whether the claim is directed toward at least one of the enumerated subject matter categories – a process, a machine, a manufacture or a composition of matter. Next, the Examiner should determine whether the claim is directed to an excluded subject matter, which are: a law of nature, a natural phenomenon, or an abstract idea. The Guidelines further clarify, if the claimed invention produces a result that is tied to the physical world that does not preempt the judicial exception,

then the claim meets the statutory requirement. If the Examiner does not find such a practical application, the claims are deemed nonstatutory.

The examination guidelines suggest that one way to avoid a rejection based on excluded subject matter is to present a claim that is directed to a “practical application.” Under the guidelines, there are two ways to determine whether a practical application claim falls within the safe harbor of practical application for excluded subject matter. One way is to determine whether the claimed invention transforms an article to a different state or thing. **The alternate way, is to determine whether the claimed invention otherwise produces a useful, tangible and concrete result.** A useful result is one that is specific, substantial and credible. Tangible results are a real world result. Concrete results are those that can be repeatable.

The claims are devoted to a method. Therefore the first requirement under the guidelines, that the claims must recite and enumerate subject matter, is satisfied.

Now the attention needs to be turned to the second requirement. That is, whether the claim is directed to an excluded subject matter which are: a law of nature, a natural phenomenon, or an abstract idea. As the guidelines further provide, this prong can be satisfied if the claimed invention produces a result that is tied to the physical world that does not preempt the judicial exception. Under the guidelines, there are two ways to determine whether a practical application claim falls within the safe harbor of practical application for excluded subject matter. As noted by the guidelines, an alternate way, is to determine whether the claimed invention otherwise produces a useful, tangible and concrete result. The present invention at least satisfies the alternate way, thereby satisfying the second requirement.

The present invention produces a useful result. As noted in the background section of the Specification, to compare gene expression data between samples, this data needs to be normalized. A skilled artisan would know as to why gene expression data needs to be compared. The Examiner notes on page 4 of the Office Action, that data need not be normalized for being used. However, this is believed to be an irrelevant and incorrect argument in support of the proposition that normalizing data is not useful. In fact, as noted in the Specification, a significantly better comparison can be made between data if they are normalized. Notably, by normalizing data, the comparison is made against a same reference value. The preambles of the claims clearly specify that the methods are used for normalizing data. Further, the claim specifies a normalized result that is produced.

The present invention produces a tangible result. For example, as noted above, a normalized data is produced which can lead to a better comparison of data. This is a tangible result.

There is nothing to indicate that the results cannot be repeatable. Therefore the present invention produces a concrete result.

As noted above, all the prongs of the new USPTO Guidelines are satisfied. The Examiner's finding of nonstatutory subject matter should be withdrawn.

***Claim rejections under 35 U.S.C. § 112***

The claims have been amended to further clarify the subject matter of the invention. In relation to the method step "indicating...", the Examiner seeks clarification of whether this is a method step. The Applicants respectfully submit that this is indeed the case.

Further, regarding the method step "calculating a coefficient...", the Examiner contends that it is unclear as to what way the coefficient is calculated. Referring to the Fig. 1 and the accompanying description in the Specification, it should be clear to a skilled artisan that "a" is the intercept between the line 4 and the vertical axis, and as shown in equations 2 and 3;  $10^a$  is the coefficient corresponding to claim 1. Likewise, in relation to Fig. 3, it is clear that the slope of the line 10 is the coefficient of claim 3.

***Claim rejections under 35 U.S.C. § 102***

Rejection of claims 3 and 4 under 35 U.S.C. 102(a) and (e) based on Li et al.

In rejecting claims 3 and 4, the Examiner refers to items (17) and (19) of Li which are reproduced below:

With linear normalization, it is assumed that the intensities between two or more arrays are related as a straight line with a zero y-intercept. Its use leads to multiplication by a scaling factor (slope of the line) to make the mean of the "experiment" chip the same as that of the baseline chip..A description of this technique applied to Affymetrix probe arrays is given by Alon et al. (1999). For example, see page 6746, lines 2-4 which states that

"To compensate for possible variations between arrays, the intensity of each EST on an array was divided by the mean intensities of all ESTs on that array and multiplied by a nominal average intensity of 50."

Ignoring the slight differences of the number of retained probe pairs per gene (due to outlier probe removal), the essential effect of these operations is equivalent to the multiplication of each probe pair difference by a constant scaling factor.

Chen et al. (1998) describe an application of the linear normalization technique to cDNA spotted arrays, where one intensity channel is normalized against

another on the same array. For example, on page 371, formulae (12) & (13) represent a linear scaling operation across the whole array.

The Applicants respectfully submit that the above described linear normalization is completely different from the present invention. Specifically, Li does not disclose (or suggest) indicating data concerning expression quantities for two samples with points plotted on a logarithmic coordinate system where the horizontal axis represents logarithms of the expression quantities obtained for the first sample and the vertical axis represents logarithms of the expression quantities obtained for the second sample.

Further, Li does not disclose (or suggest) calculating a coefficient from a value of an intercept of an approximate straight line, on the vertical axis where the straight line is an approximation of the plotted points. Still further, Li does not disclose (or suggest) performing division processing for dividing the data concerning the expression quantities for the second sample, by the coefficient.

To anticipate a claim, each and every step of the claim should be disclosed explicitly (or inherently) in the cited reference. Li does not disclose (or suggest) the present invention at least because of the above-noted differences.

***Claim rejections under 35 U.S.C. § 103***

**Rejection of claims 1-4 under 35 U.S.C. 103(a) based on Li et al. in view of Tseng et al. and Quackenbush**

The Examiner admits that Li does not represent the data in logarithmic coordinates as required by claim 1. However, Tseng allegedly overcomes this deficiency. The Applicants disagree.



First of all, the only difference between the techniques recited in claims 1 and 3 is not that the data is represented in a logarithmic scale in claim 1. The scaling factor in claim 3 is based on the slope of the line that approximates the data, while at the same time passing through the origin. On the other hand, in claim 1, the scaling factor is a coefficient that is based on an intercept of a best fit straight line with slope 1 that intersects the vertical axis.

Further, Tseng's method is completely different. In Tseng, a quality measure for each gene is determined and a quality filtering is performed. Further a logarithm of the ratios of the values of Cy5 labeled and Cy3 cDNAs are computed. Then a square root of the sum of the logarithms of the values of Cy5 labeled and Cy3 labeled cDNA are computed for each spot. After that, a slide-specific normalization curve is fitted and normalized log ratios are computed. Subsequently, the log ratios are averaged to compute the gene effect.

Quakenbush does not overcome the deficiencies noted above in the combined teachings of Li and Tseng.

As can be seen, the combined teachings of Li, Tseng and Quakenbush does not suggest the present invention (as recited on claims 1 and 2). Specifically, the combined teachings do not suggest a straight line with slope 1 that is an approximate representation of the data. Further, the combined teachings do not suggest determining an intercept of this line with the vertical axis. Still further, the combined teachings do not suggest performing a division with a coefficient based on the intercept.

A skilled artisan would not have been able to practice the present invention (as recited in claims 1-4) based on the combined teachings of Li, Tseng and Quakenbush.

AMENDMENT UNDER 37 C.F.R. § 1.11  
U.S. Application No.: 10/671,546

Attorney Docket No.: Q77645

***Claim rejections under 35 U.S.C. § 103***

Rejection of claims 1-2 under 35 U.S.C. 103(a) based on Tseng et al. in view of Alon et al.

The Applicants reiterate the arguments noted above regarding the differences between Tseng and the present invention. Further, Alon does not overcome the deficiencies noted above in the teachings of Tseng.

***New Claims***

The Applicants respectfully submit new claims 5-8 for examination.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

*Ray S. Iyer #1  
43,078 &*

SUGHRUE MION, PLLC  
Telephone: (202) 293-7060  
Facsimile: (202) 293-7860

WASHINGTON OFFICE

**23373**

CUSTOMER NUMBER

Chid S. Iyer  
Registration No. 43,355

Date: September 20, 2006